● CHOICE OF PSYCHIATRIC CRITERIA AFFECTS RELATIONSHIP BETWEEN NON-CARDIAC CHEST PAIN (NCCP) AND PANIC DISORDER (PD). L.A. Bradley, I. Scarinici, J.E. McDonald, C.A. Schan, J.E. Richter. Depts of Med. and Psychology, Univ. of Ala. Birmingham, Birmingham, AL 35294.

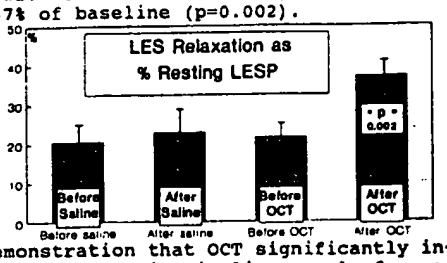
Psychiatric studies have shown that 34%-59% of NCCP patients suffer PD; this anxiety disorder may underlie their pain and disability. These studies used patients with coronary artery disease (CAD) as controls and often used liberal PD criteria. We performed the first study of the relationship between NCCP and PD using both stringent and liberal published criteria and 4 control samples consisting of patients with CAD, irritable bowel syndrome (IBS), reflux disease (GERD), and healthy persons (HC). METHODS AND RESULTS: A structured psychiatric interview, the Diagnostic Interview Schedule, was administered to consecutive paid volunteers to obtain samples of 17 NCCP's (4 M, 13 F, mean age 46.5), 12 IBS's (2 M, 10 F, mean age 41.8), 12 CAD's (8 M, 4 F, mean age 65.2), 20 GERD's (10 M, 10 F, mean age 44.6) and 18 HC's (8 M, 10 F, mean age 44.5). The subject samples were equivalent in education level although CAD's were significantly older than other samples ($p < .05$). Presence or absence of PD determined using 3 criteria: (a) stringent "DSM-III" criteria of anxiety or fear episodes, ≥ 4 of 12 specific physical symptoms (e.g. sweating), and ≥ 3 attacks in a 3-week period; (b) liberal "No Fear PD" criteria of sudden episodes of at least 1 of 4 specific physicial symptoms (e.g., rapid heartbeat), ≥ 4 other DSM-III physical symptoms, and ≥ 3 attacks in 3-week period); and (c) liberal "Simple PD" with all criteria in No Fear PD except those for attack frequency. $\chi^2$ analyses compared PD frequency across samples with the 3 criteria.

| | HC | CAD | NCCP | IBS | GER | P |
|---|---|---|---|---|---|---|
| No PD | 17 (94%) | 12 (100%) | 13 (76%) | 10 (83%) | 18 (90%) | 0.29 |
| DSM-III | 1 (6%) | 0 (0%) | 4 (24%) | 2 (17%) | 2 (10%) | |
| No PD | 17 (94%) | 11 (92%) | 9 (53%) | 8 (67%) | 15 (75%) | 0.03 |
| No Fear PD | 1 (6%) | 1 (8%) | 8 (47%) | 4 (23%) | 5 (25%) | |
| No PD | 15 (83%) | 8 (67%) | 4 (24%) | 6 (50%) | 12 (60%) | 0.01 |
| Simple PD | 3 (17%) | 4 (33%) | 13 (76%) | 6 (50%) | 8 (40%) | |

PD more frequent among NCCP's than HC's ($p<.01$) only when liberal PD criteria used: CAD's, IBS's and GERD's did not differ from HC's with any criteria. Liberal criteria produced much greater frequencies of PD among IBS's and GER's than the 16% rate (DSM-III) seen with chronic pain. CONCLUSIONS: 1) PD differentiates NCCP's from HC's only when liberal criteria used; 2) liberal PD criteria produce large increases in PD diagnoses; 3) liberal PD criteria should be used cautiously since PD can be artifact of physical symptoms associated with chronic pain.

● SOMATOSTATIN ANALOGUE (OCTREOTIDE) INHIBITS LOWER ESOPHAGEAL SPHINCTER RELAXATION. M.S. Branch, F.M.Gessner, J.W.Smith, S.R.Brazer. Duke University Medical Center, Durham, NC.

Lower esophageal sphincter relaxation (LESR) may be mediated by the neurotransmitter vasoactive intestinal peptide (VIP). Because octreotide (OCT) inhibits VIP release, we performed a double-blind, placebo-controlled crossover study in volunteers to test the hypothesis that OCT inhibits LESR. Ten subjects were necessary to detect a 25% change in LESR (alpha=0.05, beta=0.20, two-sided test). Twenty wet swallows were recorded using a Dent sleeve before and after either IV saline or 50 mcg OCT on two separate days in random order. LESR was expressed as a percentage of resting LES pressure (LESP). The paired differences in LESR after saline and OCT for each subject were analyzed with a Wilcoxon sign rank test. RESULTS: Resting LESP averaged 23.8 mm Hg. LESP decreased to 22% of resting tone with wet swallows. OCT inhibited LESR, which reached only 37% of baseline (p=0.002).




Our demonstration that OCT significantly inhibits LES relaxation implies a role for somatostatin in the control of LESR. These observations may also have significance in the treatment of GER and in the use of OCT in patients with esophageal motility disorders.

ANTAGONISTIC PROPERTIES OF ICS 205-930 ON CISAPRIDE-INDUCED CONTRACTIONS OF SEGMENTS OF THE GUINEA-PIG COLON ASCENDENS. M.R. Briejer*, A.L. Meulemans**, J.A.J. Schuurkes**. *Faculty of Pharmacy, University of Utrecht, Utrecht, The Netherlands, **Department of Gastrointestinal Pharmacology, Janssen Research Foundation, B-2340 Beerse, Belgium.

On the guinea-pig ileum cisapride has been shown to enhance the responses to electrical stimulation via $5HT_4$-receptor sites. On the guinea-pig colon cisapride evokes a contractile response. The aim of our study was to determine whether this effect on the colon could also be mediated via $5HT_4$-receptors by using the $5HT_4$-receptor antagonist, ICS 205-930 (at ≥ $10^{-6}$ M). Colonic segments of about 3 cm were mounted in a 100-ml organ bath, filled with De Jalon-buffer at 37° C and gassed with carbogen (95 % $O_2$, 5 % $CO_2$). The preload was 2 g, and the responses were measured isotonically.

Cisapride evokes maximal contractions of 43 ± 3 % of the methacholine (3 x $10^{-7}$ M)-induced responses, the maximal contraction being reached at 3 x $10^{-7}$ M cisapride ($EC_{50}$ = 1.1 x $10^{-7}$ M). In the nanomolar range, ICS 205-930 has $5HT_3$-antagonistic properties. Cisapride was not significantly inhibited at ICS 205-930 concentrations of 1 x $10^{-7}$ M. In the micromolar range however, ICS 205-930 also antagonizes $5HT_4$-receptor agonists. ICS 205-930 in a concentration of 3 x $10^{-6}$ M inhibited the cisapride-induced response with 85 %. At this concentration of ICS 205-930, the methacholine-induced contraction is also inhibited by 15 %. At higher concentrations the methacholine-response is seriously affected. ICS 205-930 itself induces small contractions (5-10 %) at concentrations ≥ 3 x $10^{-6}$ M.

Conclusions: ICS 205-930 is able to antagonize cisapride-induced contractions on the guinea-pig colon ascendens in the micromolar range. This might indicate that cisapride acts as a $5HT_4$-agonist on the guinea-pig colon. A selective $5HT_4$-receptor antagonist however is still not available.

● GALLBLADDER MUSCLE CONTRACTION RELEASES CHOLINE METABOLITES E.A. Brotschi, W.A. Vaules, N.A. Midis, and S.H. Zeisel, Depts. of Surgery and Pathology, Boston VAMC and Boston University School of Medicine

When gallbladder (GB) tissue is incubated with radioactive choline and stimulated to contract, radiolabeled choline metabolites are released. To determine whether this release represents acetylcholine (ACh) synthesis or a different metabolic pathway, we analyzed choline metabolites formed and released from the GB.

Methods: GBs removed from guinea pigs were radiolabeled in organ bath with $^{14}$C-methyl-choline (10uC/ml) for 15min. Hemicholinium, an inhibitor of choline uptake, and the cholinesterase-inhibitor eserine were in all buffers. GBs were then stimulated with cholecystokinin-octapeptide $10^{-10}$M during mechanical distension. Mucosa was removed from the GBs, and incubation buffers and muscle were extracted. Choline metabolites in the aqueous phase were analyzed by HPLC, and those in the organic phase by thin-layer chromatography.

Results: Stimulation released radiolabel from the GB, with 43± 4% of total counts released at 20 min (N=6). At 10 min, radiolabel in the buffer included choline 99±1%, and betaine 1% (N=10), while at 30 min choline decreased to 90% , and betaine increased to 9%. Analysis of the GB muscle immediately after labeling showed radiolabel contained in choline 51±8%, betaine 15±6%, and phosphocholine 27±5% (N=4). Phosphocholine increased to 37±6% (N=6) after 20min, and continued to increase with longer incubations. ACh constituted no more than 1-2% of radiolabel in the tissue, and was not identified in any buffers (N=10). To check for ACh hydrolysis, control incubations were performed with $^{14}$C-ACh added to the bath. At time zero, 73±8% of added ACh was recovered from the buffer, and after 10 min of incubation 60±11% was recovered (N=4).

Conclusions: Contrary to expectations, the major $^{14}$C-choline metabolite released during contraction was choline, and no ACh was identified in the bath. $^{14}$C-Choline in the GB muscle was stored in a readily-released pool, and metabolized into betaine and phosphocholine. Phosphocholine is an intermediate in the formation of phosphatidylcholine, and may accumulate in GB muscle because the cytidylyltransferase step in this pathway is normally rate-limiting.